

# Postsurgical tetanus

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The incidence of tetanus declined dramatically in the 20th century owing to routine vaccination and prompt attention to wound care. Postsurgical tetanus is uncommon, with both exogenous and endogenous sources being responsible for disease. The majority of cases of postoperative tetanus have been observed after intra-abdominal surgery. Those at high risk for developing tetanus include immigrants, the elderly, injection drug users, patients with diabetes and people of Hispanic ethnicity. Although most patients with tetanus can recover if managed appropriately, prevention through active and passive immunization is the main goal. This paper reviews postsurgical tetanus and provides an approach to its prevention and treatment.

La vaccination de routine et le traitement rapide des plaies ont réduit de façon spectaculaire l'incidence du tétanos au cours du XXe siècle. Le tétanos postchirurgical est rare et des sources à la fois exogènes et endogènes sont à l'origine de la maladie. On a observé la majorité des cas de tétanos postopératoire après une intervention chirurgicale intra-abdominale. Les personnes qui présentent un risque élevé de tétanos comprennent les immigrants, les personnes âgées, les utilisateurs de drogues injectables, les patients atteints de diabète et les personnes d'origine ethnique hispanique. Même si la plupart des patients atteints de tétanos peuvent se rétablir à condition de recevoir le traitement approprié, la prévention par l'immunisation active et passive constitue le but principal. Cette communication passe en revue le tétanos postchirurgical et présente une stratégie de prévention et de traitement.

**T**etanus is a potentially lethal but preventable disease caused by the exotoxin of *Clostridium tetani*. It continues to be an important problem in the developing world, where 50% of cases are neonatal, with a mortality of up to 90%. Almost all originate with contamination of the umbilical stump in infants born to mothers who are not immune.

Tetanus is uncommon in developed countries. Epidemiological data indicates that 0%–3.5% of all reported cases occur postoperatively, most frequently after intra-abdominal surgery.<sup>1–7</sup> This translates into averages of about 1 (reported) case every 7 years in Canada, and 1 every year in the USA.

## Incidence and trends

In North America, the number of reported cases of tetanus has declined substantially over the past 30 years. From 1989 through 2000 in Canada, it ranged from 2 to 7 per year (Table 1).<sup>8</sup> In 1965, there were about 300 cases reported in the USA, which declined to about 40 in 2000.<sup>9</sup> The average incidence there in 1947 was 3.9 cases per million person-years, compared with 0.16 during 1998–2000.<sup>9</sup>

The number of tetanus cases derived from passive reporting by physicians may significantly underestimate the true incidence rate of tetanus in Canada and the USA.<sup>9</sup> Of an estimated 1100–2300 cases that occurred between 1979 and 1984 in the Uni-

ted States, only 501 were reported to the Centers for Disease Control and Prevention.<sup>10</sup> Completeness of case reporting has not been evaluated recently.<sup>9</sup>

Morbidity and mortality from tetanus has declined in North America as well. The case fatality rate in the USA was 91% in 1947, compared with 18% during 1998–2000. The reductions in morbidity and mortality have resulted primarily from the 1947 introduction of tetanus antitoxin and toxoid, availability of vital supportive measures, improvement in wound care and antibiotics.<sup>9</sup>

## Disease course

Postoperative tetanus develops quick-

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ly, usually within 24 hours. When tetanus spores germinate in ischemic tissue, they produce tetanospasmin and tetanolysin. Tetanolysin can damage otherwise viable tissue surrounding the infection and optimize conditions for bacterial multiplication.<sup>11</sup> Tetanospasmin leads to the clinical syndrome of tetanus and involves 3 components of the nervous system: the central and autonomic systems and the neuromuscular junction.<sup>12</sup> Once conveyed to the spinal cord and brain via retrograde transport, tetanospasmin migrates into glycerinergeric or  $\gamma$ -aminobutyric acid (GABA)ergic neurons, preventing the release of inhibitory neurotransmitters. It disinhibits sympathetic reflexes at the spinal level and may also disrupt parasympathetic function, manifesting as autonomic instability characterized by labile changes in blood pressure and heart rate. The neuromuscular junction is permanently disabled; return of motor function requires sprouting of the motor neuron's terminal end to produce new synapses, which can take 4–6 weeks. These actions result in the cardinal features of tetanus: muscle rigidity characterized by trismus, risus sardonicus, dysphagia and opisthotonus, and reflex spasms. One of the most serious complications is airway

compromise and respiratory failure. Rhabdomyolysis can also occur. The patient's pain can be extreme.

The most important determinants of severity and prognosis of clinical tetanus are the incubation period (the interval between wounding and the emergence of symptoms) and the period of onset (the interval between the first symptom and the first spasm). An incubation period >7 days and a period of onset >48 hours are associated with a poor outcome.

### Sources of infection

Both exogenous and endogenous sources have been implicated in disease development. Dressings or equipment that are inadequately sterilized and even dust have been suspected as possible causes of postoperative tetanus.<sup>13,14</sup> In 1928, Mackie<sup>15</sup> reported 9 cases and 8 deaths in Edinburgh, in which contaminated catgut was found to be the vehicle of infection. In 1946, Robinson and coauthors<sup>13</sup> described 2 cases in which contaminated dust in the operating room (OR) was considered as a source of infection. The sterilizer was found to be efficient and samples of the dressings, talc, saline and catgut used proved to be sterile. In the first case, samples of dust from the floor, wall and fan collected the day after the implicated surgery revealed tetanus bacilli. An independent survey of the room 2 weeks later, after it had undergone careful disinfection, revealed no further tetanus bacilli. In the second case, it was samples of dust collected on sterile swabs that yielded tetanus bacilli. Robinson's group<sup>13</sup> therefore suggested measures to exclude infected dust, including wet-dusting of OR walls with antiseptic solutions, an adequate filtering system and precautions against the introduction of dust on footwear. Sevit<sup>16</sup> in 1948 described 2 other cases where goat hair that was used to prepare plaster for repairs in the OR was contaminated with tetanus spores. In a 1957 outbreak in the United Kingdom of 5 postoperative cases, tetanus

spores were isolated from sterilized gloves.<sup>17</sup>

Between 1% and 10% of people express *C. tetani* in their stool. In 1926, Wainwright<sup>18</sup> reviewed over 3000 cases of tetanus and described about 12% as postoperative. Most occurred after abdominal or gynecological surgery, and in the majority the intestinal tract was considered the source of infection. In most cases, however, firm evidence of the source involved was lacking. It is worthy of note that in many cases considered by Wainwright, tetanus followed surgery that did not penetrate the intestinal tract: 29 abdominal hysterectomies, 78 oophorectomies and 38 inguinal hernia repairs. Sixty-nine cases (19%) involved operations on the gastrointestinal tract, of which 23 were for hemorrhoids. In 1942, Calvert reported a case of tetanus in a 57-year-old woman in whom organisms were isolated from the content of a resected specimen of ileum.<sup>19</sup>

In the *Morbidity and Mortality Weekly Report* (MMWR) surveillance summary for 1991–1994 in the USA,<sup>6</sup> 2.2% of patients for whom information on medical care was reported developed tetanus after an abdominal laparotomy. In 1995–1997,<sup>7</sup> 1 reported US case of tetanus occurred after a 63-year-old woman underwent a hemorrhoidal banding procedure. No American cases of tetanus after intra-abdominal surgery were reported in the 1998–2000 MMWR summary.<sup>9</sup> But in 2000, a case of postoperative tetanus after urgent laparotomy, pyloroplasty and oversewing of a duodenal ulcer to correct massive upper gastrointestinal bleeding was reported in Toronto.<sup>20</sup>

Tetanus rarely occurs after clean surgery. Luisto<sup>21</sup> in 1993 reported tetanus in a man with a closed trimalleolar fracture of his right ankle, which was fixated with screws before application of a plaster cast. The source of the infection in the OR could not be identified. In 1994, Ruiz-Santana and colleagues<sup>22</sup> de-

**Table 1**  
**Reported cases of tetanus in Canada, 1989–2000**

Year	Number of cases
1989	2
1990	4
1991	2
1992	4
1993	7
1994	3
1995	6
1996	3
1997	3
1998	2
1999	7
2000	3

1991–2000 data are from Health Canada's Notifiable diseases on-line ([http://dsol-smcd.hc-sc.gc.ca/dsol-smcd/ndis/disease2/tetn\\_e.html](http://dsol-smcd.hc-sc.gc.ca/dsol-smcd/ndis/disease2/tetn_e.html)).

scribed a 68-year-old farmer who developed tetanus after replacement of an aortic-bifemoral prosthetic graft. In this presumably clean surgery the source of the infection went undetermined, although it was hypothesized that spores were previously introduced and remained localized in an area of low potential for oxygen reduction (redox) favoured by the presence of devitalized tissue from severe peripheral vascular disease.

Necrosis, secondary infection, and foreign bodies such as surgical clips and sutures can facilitate growth of the organism.<sup>7</sup> In 1995, a Chinese immigrant in Toronto developed tetanus after repair of his left Achilles tendon.<sup>23</sup> A plastic spacer had been inserted during the operation. The patient had never been immunized, as evidenced by an absence ( $<0.01$  IU/mL) of protective antitoxin in his serum. The presence of a foreign body may have been an important factor, resulting in a low redox potential and allowing spore germination. The originating source of the spores was unclear, although exogenous sources such as dust, equipment or the cast should have been considered. Unfortunately, no swabs or cultures were taken from the OR. Apparently, no further cases have since been reported from the same OR or at that hospital; clustering of cases would have suggested an exogenous source of disease.

Patients at high risk include immigrants, the elderly, those with diabetes, injection drug users (IDUs) and people of Hispanic ethnicity.<sup>9</sup> Older adults and immigrants may be unvaccinated or inadequately vaccinated. The immune response to toxin can also be less robust with increasing age, especially in those with chronic conditions.<sup>9</sup> Diabetics may be more prone to tetanus because of their predisposition to peripheral vascular disease and peripheral neuropathy. In IDUs, contaminated drugs, unsanitary injection equipment and practices (e.g., needle sharing) and altered immunity might increase

their risk. The high incidence of tetanus in 1998–2000 in the USA among Hispanic patients was partly attributable to cases in IDUs, many of whom were Hispanic.<sup>9</sup>

### Disease management

Because the isolation of organisms from wounds is neither sensitive nor specific, tetanus remains a clinical diagnosis. Anerobic culture of tissue or aspirates isolates the organism in about 30% of cases, and the organism may be grown from wounds in the absence of clinical signs and symptoms.<sup>24</sup>

If optimally managed, any patient, regardless of age or severity of tetanus, has a chance of full recovery. This is true even with delayed recognition of the disease. The treatment of tetanus is directed toward neutralization of the circulating toxin, debridement of the wound site, control of muscle spasms and autonomic dysfunction, and supportive intensive care. The most important early goals of treatment are airway and ventilatory control with possible neuromuscular blockade, administration of antispasticity agents and passive immunotherapy with tetanus immunoglobulin.

Antispasticity agents include neuromuscular blocking agents, benzodiazepines and the more recent option of intrathecal baclofen.<sup>25,26</sup> Baclofen, a GABA-receptor agonist, does not cross the blood-brain barrier and requires administration into the subarachnoid space. Of 2 patients with tetanus who were given intrathecal baclofen for spasms,<sup>25</sup> 1 developed hypotension 4 hours later, requiring an infusion of adrenaline. The other developed methicillin-resistant *Staphylococcus aureus* (MRSA) meningitis, which responded to intravenous (IV) vancomycin. The authors did conclude that baclofen diminished spasticity. In a recent retrospective cohort study<sup>26</sup> conducted 1998–2003 in an intensive-care setting, 22 patients with grade III tetanus (characterized

by generalized rigidity, paroxysms of skeletal muscles and autonomic dysfunction) were given intrathecal baclofen within 72 hours after admission. An initial bolus of 40–200 µg was followed by an infusion not exceeding 80–125 mg/h. Thirteen patients developed hypotension and bradycardia. One developed *S. epidermidis* meningitis and recovered after treatment with vancomycin. One patient, who had been given a booster of tetanus vaccine only, died. With no comparison group to make this a true retrospective cohort study, firm conclusions about the role of intrathecal baclofen would be difficult to draw from this report.

A patient's tetanus antitoxin titre should be measured before administration of tetanus immunoglobulin. There is controversy as to what is considered a protective level of antibodies.<sup>20</sup> For example, in Toronto the provincial laboratory uses a cutoff of 0.1 IU/mL, whereas in Vancouver a cutoff of 0.2 IU/mL is used.

For management of acute tetanus, immunoglobulin must be given to directly neutralize free tetanospasmin as soon as the patient's airway is protected and muscle spasms are controlled.<sup>26</sup> It should be administered before surgical debridement, since free tetanospasmin may be released into the bloodstream by wound manipulation. Doses of 3000–6000 IU have been given; however, an intramuscular (IM) dose of 500 IU has been shown to be as effective as larger doses.<sup>27</sup> The half-life of tetanus immunoglobulin is around 28 days, making repeated doses unnecessary.

Toxin that has already entered the central nervous system is unaffected by administration of tetanus immunoglobulin. Because of this, intrathecal therapy with tetanus immunoglobulin has been suggested. A recent randomized controlled trial<sup>28</sup> examined 120 patients allocated to immunoglobulin by both intrathecal and IM routes ( $n = 58$ ) or IM route alone (controls,  $n = 62$ ). Doses of 1000 IU were used for intrathecal

administration and 3000 IU for the IM route. Patients in the treatment group showed better clinical progression by grade of tetanus than the control group ( $p = 0.005$ ), as well as shorter durations of spasms ( $p = 0.0001$ ), respiratory assistance ( $p = 0.01$ ) and hospital stay ( $p = 0.03$ ). The difference in relative risk of death, however, was not statistically significant. One might question if the higher total dose might have played a role in the better outcomes in the treatment group.

Antitoxin and a complete primary immunization series of 3 doses of tetanus toxoid should be administered to all patients suspected of having tetanus, even those previously vaccinated, in addition to immunoglobulin.<sup>20</sup> The amount of toxin released during even the most severe case of tetanus is insufficient to confer immunity. Toxin-neutralizing antibody can be overwhelmed if the burden of toxin is high enough, and clinical tetanus can develop.<sup>20</sup>

Antibiotics such as penicillin and metronidazole have been used to inhibit *C. tetani* growth and stop toxin production.<sup>29</sup> As penicillin could theoretically potentiate the neuroexcitatory effect of tetanospasmin by acting as a central GABA antagonist, metronidazole has been recommended as the preferential agent.<sup>30</sup> In 1985 a nonrandomized study<sup>29</sup> compared metronidazole (500 mg by mouth or 1 g rectally every 6 h for 7–10 d) with procaine penicillin (1–5 million units IM every 8 h for 7–10 d) in patients with moderate tetanus (based on incubation period, infection site, state of immunization and complicating factors). Metronidazole was more effective: patients in that group were significantly less likely to die in hospital (7% v. 24%) and more likely to have improved by day 5 (56% v. 37%); their hospital stays were also shorter (by an average of 5 d). More recently, in a randomized controlled trial in 2004, patients with varying severities of tetanus were treated with IM benzathine

penicillin (1 dose of 1.2 million units), IV benzylpenicillin (2 million units every 4 h for 10 d) or enteral metronidazole (600 mg every 6 h for 10 d).<sup>30</sup> Between-group differences in hospitalization times, in-hospital mortality, incidence of autonomic dysfunction, and requirements for sedation, tracheostomy and mechanical ventilation were not significant. (Note that procaine penicillin was used in the former study<sup>29</sup> rather than benzylpenicillin or benzathine penicillin. Procaine has been shown to have an excitatory effect on the nervous system through inhibition of GABA release.<sup>30</sup>)

Meticulous surgical debridement of all devitalized tissue and foreign bodies should also be undertaken as soon as possible, to eliminate conditions that support the growth of vegetative forms of the organism.

Autonomic dysfunction, a serious complication, can usually be managed with labetalol, clonidine, morphine or epidural anesthesia.<sup>27,31</sup>

Although mortality from this disease has declined substantially in the last 30 years, it should be stressed that prevention is the main objective. Active immunization with tetanus toxoid is one of the most effective preventive measures in medicine. Passive immunization should be considered at the time of any tetanus-prone wound if adequate prior immunization has not occurred.

When the immunization history is vague or poorly documented, the person should be considered to be non-immune. The disease itself does not confer immunity, as the amount of toxin required for lethal disease is insufficient to be immunogenic. An immunization history should be routine in the preoperative health assessment of all patients, especially those at high risk for tetanus. If someone is not adequately vaccinated, 3 immunizations with IM toxoid should be given as part of the primary series, followed by a booster every 10 years. The role of the primary care physician should include assessment of

immunization status during routine visits, well before potential exposures such as wounds or surgery. Failure to immunize may have serious medico-legal implications.

In non-immune high-risk patients undergoing emergency gastrointestinal surgery, both passive (tetanus immunoglobulin) and active immunization should ideally be given. For others undergoing gastrointestinal surgery and for clean surgery (including orthopedic cases) in the non-immune host, toxoid should be administered (as passive immunization may not be cost-effective). These recommendations are ideal, but may be impracticable.

Having a well-designed, well-maintained operating theatre is important but likewise ideal, especially for high-risk patients. If air-intake pressure is lower in the OR, spores are more likely to be present. A smooth-surfaced OR is preferable to tiles, where bacteria can accumulate in the grout. The quality of the filters and ducts should be monitored regularly and these filters and ducts maintained. It would be important to provide surgical patients, especially high-risk patients, with this type of safe surgical environment.

Tetanus spores can resist moisture exposure and extremes of temperature. Material must be kept at 100°C for 4 hours, or autoclaved at 121°C and 103 kPa for 15 minutes to ensure sterilization. Surgical technique that avoids creating devitalized tissue or allowing any to remain would also be important.

## Conclusions

Tetanus is, as described, a largely preventable disease. Despite widespread immunization of infants and children in Canada and the USA since the 1940s, tetanus, including postsurgical tetanus, still occurs in developed nations. Although uncommon, tetanus may manifest in a very severe fashion and can be fatal. However, it is unquestionable that



tetanus can and should become a disease with merely historical significance.<sup>12</sup>

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